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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/547,220 | 04/11/2000 | Michael Brines | 10165-006-999 | 4714 |
| 20583 | 7590 | 02/22/2006 | EXAMINER | |
| JONES DAY 222 EAST 41ST ST NEW YORK, NY 10017 | | | DEBERRY, REGINA M | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1647 | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|------------------------------|-------------------------------|------------------|
| Office Action Summary | Application No. | Applicant(s) |
| | 09/547,220 | BRINES ET AL. |
| | Examiner Regina M. DeBerry | Art Unit 1647 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 06 December 2005.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 28-64 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) 28-39 is/are allowed.
- 6) Claim(s) 40-51 and 64 is/are rejected.
- 7) Claim(s) 52-63 is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

| | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____. | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____. |

Status of Application, Amendments and/or Claims

The amendment filed 06 December 2005 has been entered in full. New claim 64 was added. Claims 28-64 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection to claims 33, 39, 45, 51, 57 and 63 under 35 USC 112, first paragraph, scope of enablement, as set forth at pages 3-5 of the previous Office Action (06 June 2005), is *withdrawn* in view of the amendment (06 December 2005).

The rejection to claims 33, 39, 45, 51, 57 and 63 under 35 USC 112, first paragraph, written description, as set forth at pages 6-7 of the previous Office Action (06 June 2005), is *withdrawn* in view of the amendment (06 December 2005).

The rejection to claims 28, 34, 40, 46, 52 and 58 under 35 USC 112, second paragraph, as set forth at pages 8-9 of the previous Office Action (06 June 2005), is *withdrawn* in view of the amendment and Applicant's arguments regarding the terms "increase vs. toxic increase"(06 December 2005).

The rejection to claims 28-63 under 35 USC 102(b) as being anticipated by Igari *et al.*, US Patent 5,591,713, as set forth at pages 9-10 of the previous Office Action (06 June 2005), is *withdrawn* in view of the amendment (06 December 2005).

Claim Rejections - 35 USC § 112, First Paragraph, Written Description New Matter

Claims 40 and 46 (and dependent claims 41-45, 47-51) remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. **This was a new matter rejection.** The specification as originally filed does not provide support for the invention as now claimed: "...without a **toxic** increase in hemoglobin concentration or hematocrit". The basis for this rejection is set forth at pages 7-8 of the previous Office Action (06 June 2005).

Applicant cites case law and argues that the law does not require that the specification provide support in exactly the same words as used in the claims to satisfy the written description requirements of 35 USC 112, first paragraph. Applicant cites various pages from the specification. Applicant argues that the Physicians' Desk Reference (PDR) shows that, depending on the patient population being treated with erythropoietin (EPO), different hematocrit ranges are targeted to avoid toxicity. Applicant argues that the specification makes it clear that the dosages of EPO used for modulation and protection of excitable tissue be non-toxic dosages of EPO.

Applicant's arguments have been fully considered but are not deemed persuasive. The PDR is not a substitute for a deficient disclosure. The specification teaches, "lacks the ability to increase hematocrit" or "not causing an increase in hemoglobin concentration". The specification does not provide written support for "without a toxic increase in hemoglobin concentration or hematocrit". Using the argument that the specification recites non-toxic amounts of EPO to provide support for, "without a toxic increase in hemoglobin concentration or hematocrit" is not found

persuasive. The instant claims now recite limitations which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Objections

Claims 40, 46, 52 and 58 remain objected to because of the following informalities. Claims 40/52 and 46/58 are objected to because the instant claims read on the same scope. The basis for this rejection is set forth at page 10 of the previous Office Action (06 June 2005).

Applicant states that the objection has been fully addressed in Section 4. Applicant cites *Tandon Corp. v. U.S. Int'l Trade Comm'n*, 831 F.2d 1017 (Fed. Cir. 1987). Applicant argues as long as a claim is clear and unambiguous and its scope can be understood to the skilled artisan, the difference in scope between it and other claims in a patent is not legally relevant to the question of claim definiteness.

Applicant's arguments have been fully considered but are not deemed persuasive. MPEP § 706.03(k) states that when two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. Applicant defined the meaning of the instant claims in the Section 4. Applicant argues that the phrase, "**without an increase in hematocrit**" in claims 52 and 58 means that the amount of EPO administered is

effective to exert a neuroprotective effect without a statistically significant rise in the hematocrit level of the subject. Applicant argues that the phrase, "**without a toxic increase in hemoglobin concentration or hematocrit**" in claims 40 and 46 requires that the amount of EPO administered is effective to exert a neuroprotective effect without an increase in hemoglobin concentration or hematocrit that would be toxic to the subject. This is not found persuasive. The effective amount of EPO to be administered in all of the claims will exert a neuroprotective effect without an increase in hematocrit and be non-toxic. Should claim 40 be found allowable, claim 52 will be objected to under 37 CFR 1.75, as being a substantial duplicate thereof. Should claim 46 be found allowable, claim 58 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

New Claim Rejections - 35 USC § 112, First Paragraph, Enablement

New claim 64 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant maintains that new claim 64 treating cerebral ischemia using erythropoietin (EPO) derivatives is fully enabled by the specification as originally filed. Applicant argues that the specification discloses explicit examples of specific mutoins,

variants, fragments, chemical modifications and analogs, as well as specific assays for evaluating their function as neuroprotective EPO derivatives effective for treating cerebral ischemia. Applicant argues that methods for making and testing such derivatives were known in the art and well within the purview of the skilled artisan. Applicant contends that the specification (page 32, line 25 to page 33, line 23) provides a working example in which the activity of an EPO derivative is tested for its neuroprotective activity as compared to the neuroprotective activity of recombinant EPO.

Applicant's arguments have been fully considered but are not deemed persuasive. Claim 64 broadly recites, "wherein said erythropoietin is an erythropoietin derivative". EPO derivative can broadly encompass any type of mutein, variant, fragments, chemical modifications, analogs, etc. The specification does not teach how to make and use **any EPO derivative that is effective to exert a neuroprotective effect upon peripheral administration for treating cerebral ischemia** (Emphasis added). The instant specification fails to indicate that a representative number of structurally related compounds are disclosed and therefore, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claim and would not know how to make them for the instant method. It would require an indeterminate quantity of fundamentally unpredictable investigational experimentation of the skilled artisan to determine whether any EPO derivative could be used in the same manner as the native exemplar (exerting a neuroprotective effect for treating cerebral ischemia). Such experimentation would be

undue for one skilled in this art. The disclosure provides no guidance as to which regions of the EPO protein would be tolerant of modification and which would not, and it provides no working example of any variant sequence which would be within the claims. This is proven by Applicant's argument regarding an EPO derivative which is tested for neuroprotective activity. A 17-mer derived from EPO (reported to have neurotropic activity) had no effect in protection against injury in the animal model (page 33, lines 5-14). Thus, it is in no way predictable that randomly selected mutations, deletions, etc. in the disclosed sequence would afford a protein having activity (exerting a neuroprotective effect for treating cerebral ischemia) comparable to the one disclosed.

Due to the large quantity of experimentation necessary to make and test any EPO derivative for exerting a neuroprotective effect for treating cerebral ischemia in a mammal subject, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding structural limitations for EPO derivatives, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

New Claim Rejections - 35 USC § 112, First Paragraph, Written Description

New claim 64 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant argues that EPO derivatives were well known to the skilled artisan at the time of the filing of the instant application, and no undue experimentation is necessary to make and use such EPO derivatives in the methods disclosed in the instant application. Applicant contends that the specification provides actual examples of EPO derivatives that can be used in the claimed methods, and incorporates by reference issued U.S. patents containing numerous well known EPO derivatives, and methods for making such derivatives. Applicant cites case law and the Written Description Requirements Guidelines. Applicant discusses *Fiddes v. Baird* (cited by the Examiner in the last Office Action). Applicant asserts that in *Fiddes*, the patentee attempted to claim all mammalian FGF's with only the disclosure of one sequence, to support the generic claim. Applicant argues that the present claims do not encompass any EPO derivative, but, rather, encompass only those EPO derivatives that have the specific characteristic of being capable of exerting a neuroprotective effect.

Applicant's arguments have been fully considered but are not deemed persuasive. The references cited by Applicant do not teach an EPO derivative correlative with the function of exerting a neuroprotective effect for treating cerebral ischemia. The only factors present in the instant claim are a requirement that the sequence be an EPO derivative and a requirement that the EPO derivative have the activity of exerting a neuroprotective effect for treating cerebral ischemia. The claims are drawn to a genus of polypeptides that are defined only by a functional activity. As

was stated in the previous Office Action, adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. In the instant case, recombinant EPO has been disclosed, but no EPO derivatives have been disclosed, **which have the recited activity**. There is no identification of any particular portion of the structure that must be conserved in order to conserve the required function. There is no structural element correlative with the function. The specification does not demonstrate possession of the instant process steps, which require the use of undisclosed compounds. Clearly, such does not constitute disclosure of a representative number of examples of, nor adequate written description for, the claimed genus.

New Claim Objections

Claims 53-57 and 59-63 are objected to for depending from an objected claim.

Conclusion

Claims 40-51 and 64 are rejected.

Claims 52-63 are objected to.

Claims 28-39 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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